RAW SEQUENCE LISTING

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) no errors detected.

Application Serial Number:	10/559.647
Source:	IFWP
Date Processed by STIC:	12/16/05

ENTERED



IFWP

RAW SEQUENCE LISTING DATE: 12/16/2005
PATENT APPLICATION: US/10/559,647 TIME: 15:39:57

Input Set : A:\ISPH0595USASEQ.txt

```
3 <110> APPLICANT: Isis Pharmaceuticals Inc.
              Rosanne M. Crooke
              Mark J. Graham
      7 <120> TITLE OF INVENTION: MODULATION OF APOLIPOPROTEIN(A) EXPRESSION
      9 <130> FILE REFERENCE: ISPH-0595WO2
C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/559,647
C--> 11 <141> CURRENT FILING DATE: 2005-12-02
     11 <150> PRIOR APPLICATION NUMBER: 09/923,515
     12 <151> PRIOR FILING DATE: 2001-08-07
     14 <150> PRIOR APPLICATION NUMBER: 60/475,402
     15 <151> PRIOR FILING DATE: 2003-06-02
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     20 <211> LENGTH: 20
     21 <212> TYPE: DNA
     22 <213> ORGANISM: Artificial Sequence
     24 <220> FEATURE:
     25 <223> OTHER INFORMATION: Antisense Oligonucleotide
     27 <400> SEQUENCE: 1
     28 tecgteateg etecteaggg
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     31 <210> SEQ ID NO: 2
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     33 <212> TYPE: DNA
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     36 <220> FEATURE:
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     44 <211> LENGTH: 20
     45 <212> TYPE: DNA
     46 <213> ORGANISM: Artificial Sequence
     48 <220> FEATURE:
     49 <223> OTHER INFORMATION: Antisense Oligonucleotide
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     57 <212> TYPE: DNA
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     60 <220> FEATURE:
     61 <221> NAME/KEY: CDS
     62 <222> LOCATION: (46)...(13692)
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Input Set : A:\ISPH0595USASEQ.txt

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66	•																
67														1			
	_		_	ctt						_			_	_			105
70	Glu	Val	Val	Leu	Leu	Leu	Leu	Leu	Phe	Leu	Lys	Ser	Ala	Ala	Pro	Glu	
71	5					10					15					20	
				gtg													153
74	Gln	Ser	His	Val	Val	Gln	Asp	Cys	Tyr	His	Gly	Asp	Gly	Gln	Ser	Tyr	
75					25					30					35		
77	cga	ggc	acg	tac	tcc	acc	act	gtc	aca	gga	agg	acc	tgc	caa	gct	tgg	201
78	Arg	Gly	Thr	Tyr	Ser	Thr	Thr	Val	Thr	Gly	Arg	Thr	Cys	Gln	Ala	Trp	
79				40					45					50			
			_	aca									_				249
82	Ser	Ser	Met	Thr	Pro	His	Gln	His	Asn	Arg	Thr	Thr	Glu	Asn	Tyr	Pro	
83			55					60					65				
				ttg													297
86	Asn	Ala	Gly	Leu	Ile	Met	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Ala	Val	Ala	
87		70					75					80					
	_			tgt		-		_			_			-			345
90	Ala	Pro	Tyr	Cys	Tyr	Thr	Arg	Asp	Pro	Gly	Val	Arg	Trp	Glu	Tyr	Cys	
91	85					90					95					100	
		_	_	caa	_		_	-									393
94	Asn	Leu	Thr	Gln	Cys	Ser	Asp	Ala	Glu	Gly	Thr	Ala	Val	Ala	Pro	Pro	
95					105					110					115		
				ccg													441
98	Thr	Val	Thr	Pro	Val	Pro	Ser	Leu		Ala	Pro	Ser	Glu		Ala	Pro	
99				120					125					130			
																a cag	489
		: Glu		_	y Pro	Gly	Val			ı Cys	Tyr	His			Gly	/ Gln	
103			13!					140					145				
																caa	537
		_		g GTA	Thr	Tyr			Thr	· Val	. Thi			Thr	Cys	s Gln	
10		150					155					160					
																a tac	585
			Se	r Ser	Met			His	Ser	His		_	Thr	Pro	GI	Tyr	
	L 165					170					175					180	622
						_		_			_					gct	633
	_	Pro) Ası	n Ala	_		тте	Met	Asr	_	_	s Arg	, Asr	Pro		Ala	
119					185					190					199		601
																g gag	681
		Ala	t Ale		_	cys	TYT	ınr	_	_	Pro	о сту	val	_	_	Glu	
119				200			.	. 	205					210		. ~	700
																gcg	729
		Суя			ı ınr	GIN	cys) AIS	ı GIL	т стХ			va.	Ala	
123			219					220					225				777
																a caa	777
126	Pro) PT(נחו כ	r Val	. ınr	Pro	val	Pro	ser	. ∟eï	ιGIL	т нта	LPIC	, ser	. GII	1 GID	
127		230					235					240					

Input Set : A:\ISPH0595USASEQ.txt

129	gca	ccg	act	gag	caa	agg	cct	ggg	gtg	cag	gag	tgc	tac	cat	ggt	aat	825
130	Ala	Pro	Thr	Glu	Gln	Arg	Pro	Gly	Val	Gln	Glu	Cys	Tyr	His	Gly	Asn	
	245					250					255					260	
	gga																873
134	Gly	Gln	Ser	Tyr	Arg	Gly	Thr	Tyr	Ser	Thr	Thr	Val	Thr	Gly	Arg	Thr	
135					265					270					275		
137	tgc	caa	gct	tgg	tca	tct	atg	aca	cca	cac	tcg	cat	agt	cgg	acc	cca	921
138	Cys	Gln	Ala	Trp	Ser	Ser	Met	Thr	Pro	His	Ser	His	Ser	Arg	Thr	Pro	
139				280					285					290			
141	gaa	tac	tac	cca	aat	gct	ggc	ttg	atc	atg	aac	tac	tgc	agg	aat	cca	969
142	Glu	Tyr	Tyr	Pro	Asn	Ala	Gly	Leu	Ile	Met	Asn	Tyr	Cys	Arg	Asn	Pro	
143			295					300					305				
	gat																1017
146	Asp	Ala	Val	Ala	Ala	Pro	Tyr	Cys	Tyr	Thr	Arg	Asp	Pro	Gly	Val	Arg	
147		310					315					320					
	tgg			_		_	_		_		_	_	-			-	1065
150	\mathtt{Trp}	Glu	Tyr	Cys	Asn	Leu	Thr	Gln	Cys	Ser	_	Ala	Glu	Gly	Thr	Ala	
	325					330					335					340	
	gtc			_		_		_	_								1113
154	Val	Ala	Pro	Pro	Thr	Val	Thr	Pro	Val		Ser	Leu	Glu	Ala		Ser	
155					345					350					355		
	gaa																1161
158	Glu	Gln	Ala		Thr	Glu	Gln	Arg		Gly	Val	Gln	Glu	-	Tyr	His	
159				360					365					370			
	ggt																1209
	Gly	Asn	_	Gln	Ser	Tyr	Arg		Thr	Tyr	Ser	Thr		Val	Thr	Gly	
163			375					380					385				
	aga																1257
	Arg		Cys	GIn	Ala	Trp		Ser	Met	Thr	Pro		ser	His	ser	Arg	
167		390					395					400					1205
	acc																1305
	Thr	Pro	GIU	Tyr	Tyr		Asn	Ата	GIY	ьeu		мет	Asn	Tyr	Cys		
	405					410					415					420	1252
	aat																1353
	Asn	PIO	Asp	Ala		Ата	AT.d	PIO	ı yı		TYL	- 1111	Arg	Asp	435	Gry	
175			- ~~	~~~	425	+~~	224	a+ a	200	430	+ ~ ~	+ 42	~~~	~~~		~~~	1401
	gtc Val																1401
179	vai	Arg	пр	440	ıyı	Cys	ASII	ьeu	445	GIII	Cys	ser	Asp	450	GIU	Gry	
	act	~~~	~+ ~		aat	~~~	20+	~++		~~~	~++	a aa	200		~~~	act	1449
101	Thr	712	Val	712	Dro	Dro	Thr	y	Thr	Dro	Wal	Dro	Sar	T.011	Glu	212	1447
183	1111	мта	455	Ата	FIO	FIO	1111	460	1111	FIO	vai	FIO	465	пец	GIU	AIG	
	cct	taa		C 2 2	aca	aaa	act		caa	agg	cct	aaa		cac	aaa	tac	1497
	Pro		_		_	_		-						_		_	1407
187	FIU	470	GIU	GIII	AIa	FIO	475	GIU	GIII	nr 9	rio	480	Vai	GIII	Olu	Cys	
	tac		aat	aat	aas	cac		tat	cas	aac	aca		t.cc	acc	act	atic	1545
	Tyr																-5-5
	485		O T Y		O ± Y	490	~C1	- y -	**** 3	- I	495	-1-				500	
	aca	aas	ace	acc	tac		act	taa	tca	tct		aca	cca	cac	tca		1593
195	uca	224	uga	ucc	-3-	Cuu	500	-23	COU		~~9		Ju		9		

Input Set : A:\ISPH0595USASEQ.txt

194 195	Thr	Gly	Arg	Thr	Cys 505	Gln	Ala	Trp	Ser	Ser 510	Met	Thr	Pro	His	Ser 515	His	
197	agt	caa	acc	cca	gaa	tac	tac	cca	aat	act	aac	tta	atc	atg	aac	tac	1641
	Ser				_					_				_			
	261	Arg	TIIL		GIU	TYL	ıyı	PIO		AIG	Gry	шец	116		YOII	ıyı	
199				520					525					530			
	tgc																1689
202	Cys	Arg	Asn	Pro	Asp	Ala	Val	Ala	Ala	Pro	Tyr	Cys	Tyr	Thr	Arg	Asp	
203			535					540					545				
205	ccc	gat	atc	agg	taa	gag	tac	tac	aac	cta	acq	caa	tac	tica	gac	gca	1737
	Pro		-														
	FIO	_	vai	лгд	пр	GIU	_	Cys	ASII	пси	1111		Cys	Der	АЗР	AIU	
207		550					555					560					
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210	Glu	Gly	Thr	Ala	Val	Ala	Pro	Pro	Thr	Val	Thr	Pro	Val	Pro	Ser	Leu	
211	565					570					575					580	
213	gag	act	cct	tcc	qaa	caa	qca	cca	act	gag	caa	agg	cct	aaa	ata	caq	1833
	Glu																
215	020				585	0				590		5		V-1	595	V	
									4_								1001
	gag	-						_	_								1881
218	Glu	Cys	Tyr	His	Gly	Asn	GIA	GIn	Ser	Tyr	Arg	GLY	Thr	Tyr	Ser	Thr	
219				600					605					610			
221	act	gtc	aca	gga	aga	acc	tgc	caa	gct	tgg	tca	tct	atg	aca	cca	cac	1929
	Thr	_			-		_		_				_				
223			615	2			- 2	620					625				
	tcg	ast		~~~	200	000	~~~		+ > 0	000	22t	aat		++~	ata	ata	1977
	_		-				_					-					1911
	Ser		ser	Arg	Inr	Pro		Tyr	Tyr	Pro	ASII		GIA	ьeu	тте	met	
227		630					635					640					
	aac																2025
230	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Ala	Val	Ala	Ala	Pro	Tyr	Cys	Tyr	Thr	
231	645					650					655					660	
233	agg	gat.	ccc	aat.	atc	agg	t.aa	gag	tac	tac	aac	cta	acq	caa	tac	tca	2073
	Arg	_								_		_	_				
235	nr 9	nop	110	O _T y	665	9	115	Ora	- 7 -	670	71011	LCu		0111	675	001	
																	0101
	gac																2121
	Asp	Ala	Glu	GLY	Thr	Ala	Val	Ala	Pro	Pro	Thr	Val	Thr	Pro	Val	Pro	
239				680					685					690			
241	agc	cta	gag	gct	cct	tcc	gaa	caa	gca	ccg	act	gag	caa	agg	cct	ggg	2169
242	Ser	Leu	Glu	Ala	Pro	Ser	Glu	Gln	Ala	Pro	Thr	Glu	Gln	Arq	Pro	Gly	
243			695					700					705	_		-	
	gtg	cad		tac	tac	cat	aat		aaa	cad	agt	tat		aac	aca	tac	2217
	Val																221,
	vaı		Gru	Cys	IÀI	nis	_	ASII	Gry	GIII	ser	_	Arg	GIY	TIII	ıyı	
247		710					715					720					
	tcc																2265
250	Ser	Thr	Thr	Val	Thr	Gly	Arg	Thr	Cys	Gln	Ala	Trp	Ser	Ser	Met	Thr	
251	725					730					735					740	
	cca	cac	tca	cat	agt		acc	cca	gaa	tac	tac	cca	aat	act	gac	tta	2313
	Pro																
	110	1113	JUL		745	****9	****	110	Jiu	750	- 1 -		21011	111 U	755		
255											4						2265
	atc																2361
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Input Set : A:\ISPH0595USASEQ.txt

259				760					765					770			
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	Tyr																
263			775					780					785				
265	tgc	tca	gac	gca	gaa	999	act	gcc	gtc	gcg	cct	ccg	act	gtt	acc	ccg	2457
266	Cys	Ser	Asp	Ala	Glu	Gly	Thr	Ala	Val	Ala	Pro	Pro	Thr	Val	Thr	Pro	
267		790					795					800					
269	gtt	cca	agc	cta	gag	gct	cct	tcc	gaa	caa	gca	ccg	act	gag	caa	agg	2505
270	Val	Pro	Ser	Leu	Glu	Ala	Pro	Ser	Glu	Gln	Ala	Pro	Thr	Glu	Gln	Arg	
271	805					810					815					820	
273	cct	ggg	gtg	cag	gag	tgc	tac	cat	ggt	aat	gga	cag	agt	tat	cga	ggc	2553
274	Pro	Gly	Val	Gln	Glu	Cys	Tyr	His	Gly	Asn	Gly	Gln	Ser	Tyr	Arg	Gly	
275					825					830					835		
277	aca	tac	tcc	acc	act	gtc	aca	gga	aga	acc	tgc	caa	gct	tgg	tca	tct	2601
278	Thr	Tyr	Ser	Thr	Thr	Val	Thr	Gly	Arg	Thr	Cys	${\tt Gln}$	Ala	Trp	Ser	Ser	
279		_		840					845					850			
281	atg	aca	cca	cac	tcg	cat	agt	cgg	acc	cca	gaa	tac	tac	cca	aat	gct	2649
282	Met	Thr	Pro	His	Ser	His	Ser	Arg	Thr	Pro	Glu	Tyr	Tyr	Pro	Asn	Ala	
283			855					860					865				
285	ggc	ttg	atc	atg	aac	tac	tgc	agg	aat	cca	gat	gct	gtg	gca	gct	cct	2697
286	Gly	Leu	Ile	Met	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Ala	Val	Ala	Ala	Pro	
287		870					875					880					
289	tat	tgt	tat	acg	agg	gat	ccc	ggt	gtc	agg	tgg	gag	tac	tgc	aac	ctg	2745
290	Tyr	Cys	Tyr	Thr	Arg	Asp	Pro	Gly	Val	Arg	Trp	Glu	Tyr	Cys	Asn	Leu	
291	885					890					895					900	
293	acg	caa	tgc	tca	gac	gca	gaa	ggg	act	gcc	gtc	gcg	cct	ccg	act	gtt	2793
294	Thr	Gln	Cys	Ser	Asp	Ala	Glu	Gly	Thr	Ala	Val	Ala	Pro	Pro	Thr	Val	
295					905					910					915		
	acc																2841
298	Thr	Pro	Val	Pro	Ser	Leu	Glu	Ala	Pro	Ser	Glu	Gln	Ala	Pro	Thr	Glu	
299				920					925					930			
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303			935					940					945				
	cga																2937
306	Arg	_	Thr	Tyr	Ser	Thr		Val	Thr	Gly	Arg		Cys	Gln	Ala	Trp	
307		950					955					960					
	tca		_				_		_								2985
	Ser	Ser	Met							_			Glu	\mathtt{Tyr}	_		
	965					970										980	
	aat																3033
	Asn	Ala	Gly	Leu		Met	Asn	Tyr	Cys		Asn	Pro	Asp	Ala		Ala	
315					985					990					995		
	gct																3081
	Ala	Pro	Tyr	_	_	Thr	Arg	Asp			Val	Arg	Trp			Cys	
319				1000					1009					1010			
	aac																3129
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323			1015	5				1020)				1025	5			

VERIFICATION SUMMARY

DATE: 12/16/2005 TIME: 15:39:58

PATENT APPLICATION: US/10/559,647

Input Set : A:\ISPH0595USASEQ.txt

Output Set: N:\CRF4\12162005\J559647.raw

L:11 M:270 C: Current Application Number differs, Replaced Current Application No

L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date L:1208 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:4